

10/528951**DT01 Rec'd PCT/PTC 22 MAR 2005****In the Claims**

Please amend the claims presented during the international phase as follows.

Applicant presents a full set of claims showing markups of the claims with insertions and deletions indicated by underlining and strikethrough text, respectively.

1. (Original) A method of obtaining a substantially pure cannabinoid or cannabinoid acid or a product enriched in a given cannabinoid or cannabinoid acid from a plant material, comprising:
 - i) obtaining an extract containing a cannabinoid or cannabinoid acid from a plant material;
 - ii) subjecting the extract of step (i) to a chromatographic step to produce a partially purified extract;
 - iii) dissolving the partially purified extract in a first solvent, removing any insoluble material therefrom and removing the solvent; and
 - iv) dissolving the product obtained in step iii) in a second solvent, removing any insoluble material therefrom, and removing the solvent to obtain the substantially pure cannabinoid or cannabinoid acid or the product enriched in a given cannabinoid or cannabinoid acid, wherein the first and second solvents are different, and wherein one of the first or second solvents is a solvent which is substantially more polar than the cannabinoid/cannabinoid acid which it is desired to purify, and the other solvent is a solvent which is substantially less polar than the cannabinoid/cannabinoid acid which it is desired to purify.
2. (Original) A method according to claim 1 wherein one of the solvents is an alcohol.
3. (Original) A method according to claim 2 wherein one of the solvents is methanol.
4. (Currently amended) A method according to claim 1 ~~any one of claims 1 to 3~~ wherein one of the solvents is a straight or branched chain C5-C12 alkane.
5. (Original) A method according to claim 4 wherein one of the solvents is pentane.

6. (Original) A method according to claim 5 wherein one of the solvents is pentane and the other solvent is methanol.
7. (Currently amended) A method according to claim 1 ~~any one of the preceding claims~~ wherein the extract containing a cannabinoid or cannabinoid acid obtained in step (i) is prepared by a process comprising solvent extraction of the plant material.
8. (Original) A method according to claim 7 wherein step (i) comprises dissolving the plant material in an extraction solvent, removing any insoluble material from the resultant solution and removing the solvent to form an extract containing a cannabinoid or cannabinoid acid.
9. (Currently amended) A method according to claim 7 ~~or claim 8~~ wherein the extraction solvent is a non-polar solvent, ethanol, methanol or carbon dioxide.
10. (Original) A method according to claim 9 wherein the non-polar solvent comprises a straight or branched chain C5-C12 alkane.
11. (Original) A method according to claim 10 wherein the non-polar solvent is hexane.
12. (Currently amended) A method according to claim 7 ~~or claim 8~~, wherein the extraction solvent is acidified.
13. (Original) A method according to claim 12 wherein the extraction solvent is an acidified non-polar solvent.
14. (Original) A method according to claim 13 wherein the extraction solvent is an acidified straight or branched chain C5-C12 alkane.
15. (Original) A method according to claim 14 wherein the extraction solvent is 0.1% v/v acetic acid in hexane.
16. (Currently amended) A method according to claim 1 ~~any one of claims 1 to 15~~, which includes a further step, prior to step (i), of decarboxylating the plant material.

17. (Currently amended) A method according to claim 1 ~~any one of claims 1 to 6~~ wherein the extract containing a cannabinoid or cannabinoid acid obtained in step (i) comprises a botanical drug substance derived from the plant material.
18. (Original) A method according to claim 17 wherein the botanical drug substance is prepared by a process comprising solvent extraction of the plant material.
19. (Original) A method according to claim 18 wherein the botanical drug substance is prepared by extraction with carbon dioxide.
20. (Original) A method according to claim 19 wherein the botanical drug substance is prepared by a process comprising extraction with carbon dioxide (CO₂), followed by a secondary extraction step to remove a proportion of the non-target materials.
21. (Original) A method according to claim 20 wherein the secondary extraction step is ethanolic precipitation.
22. (Currently amended) A method according to claim 20 ~~or claim 21~~ wherein the process for preparing the botanical drug substance further includes a charcoal clean-up step.
23. (Original) A method according to claim 22 wherein the botanical drug substance is prepared by a process comprising:
- i) optional decarboxylation of the plant material,
 - ii) extraction with liquid CO₂, to produce a crude botanical drug substance,
 - iii) precipitation with C1-C5 alcohol to reduce the proportion of non-target materials,
 - iv) removal of the precipitate,
 - v) treatment with activated charcoal, and
 - vi) evaporation to remove C1-C5 alcohol and water, thereby producing a final botanical drug substance.
24. (Currently amended) A method according to claim 1 ~~any one of the preceding claims~~ wherein the chromatographic step comprises column chromatography.

25. (Currently amended) A method according to claim 1 ~~any one of the preceding claims~~ wherein the chromatographic step is based on molecular sizing and polarity.

26. (Original) A method according to claim 25 wherein the chromatographic step is carried out using a Sephadex™ LH-20 matrix.

27. (Original) A method according to claim 26 wherein the chromatographic step is carried out using a 2:1 mixture of chloroform/dichloromethane as solvent.

28.-39. (Canceled)

40. (Original) A method according to claim 1 which comprises a further step v) of:
v) loading the substantially pure cannabinoid or cannabinoid acid or the product enriched in a given cannabinoid or cannabinoid acid onto a Chromabond Flash BT 12M silica cartridge column, eluting with hexane:ethyl acetate (98:2) at a flow rate of approximately 5 ml/min.

41.-91. (Canceled)

92. (New) A method of producing Δ^9 THCA crystals comprising:

i) preparing an extract of the cannabis plant material with 0.1% v/v acetic acid in hexane,

ii) filtering the resultant extract and removing solvent from the filtrate by rotary evaporation to form an extract enriched in Δ^9 THCA,

iii) passing a solution of the resulting Δ^9 tetrahydrocannabinolic acid (Δ^9 THCA) enriched extract through a column packed with Sephadex-LH20™, eluting with 2:1 chloroform/dichloromethane,

iv) collecting Δ^9 THCA rich fractions eluted from the column and removing solvent by rotary evaporation,

v) re-dissolving the crude Δ^9 THCA obtained in step iv) in methanol, removing insoluble residue by filtration and removing solvent from the filtrate by rotary evaporation, and

vi) re-dissolving the product of step v) in pentane, removing insoluble residue by filtration and removing solvent from the filtrate by rotary evaporation to produce said Δ^9 THCA crystals.

93. (New) A substantially pure preparation of Δ^9 tetrahydrocannabinolic acid (Δ^9 THCA) obtained by the method of claim 92, having a chromatographic purity of greater than 95%, more preferably greater than 96%, more preferably greater than 97% or most preferably greater than 98% by area normalisation of an HPLC profile.

94. (New) A method of producing cannabidiolic acid (CBDA) crystals from plant material comprising:

i) preparing an extract of cannabis plant material with 0.1% v/v acetic acid in hexane,
ii) filtering the resultant extract and removing solvent from the filtrate by rotary evaporation to form an extract enriched in CBDA,

iii) passing a solution of the resulting CBDA enriched extract through a column packed with a matrix of hydroxypropylated cross-linked dextrans, eluting with 2:1 chloroform/dichloromethane,

iv) collecting CBDA rich fractions eluted from the column and removing solvent by rotary evaporation,

v) re-dissolving the crude CBDA obtained in step iv) in methanol, removing insoluble residue by filtration and removing solvent from the filtrate by rotary evaporation, and

vi) re-dissolving the product of step v) in pentane, removing insoluble residue by filtration and removing solvent from the filtrate by rotary evaporation to produce said CBDA crystals.

95. (New) A substantially pure preparation of cannabidiolic acid (CBDA) crystals obtained by the method of claim 94, having a chromatographic purity of greater than 90%, more preferably greater than 92% or most preferably greater than 94% by area normalisation of an HPLC profile.

96. (New) A method of producing a semi-solid preparation of Δ^9 tetrahydrocannabinolic acid (Δ^9 THC) comprising:

i) obtaining an ethanolic solution of a botanical drug substance from decarboxylated cannabis plant material,

ii) passing the solution obtained in step i) through a column of activated charcoal, and collecting the eluate,

iii) remove solvent from the eluate by rotary evaporation to give a Δ^9 THC enriched fraction,

iv) passing a solution of the resulting Δ^9 THC enriched extract through a column packed with Sephadex LH20, eluting with 2:1 chloroform/dichloromethane,

v) collecting Δ^9 THC rich fractions and removing solvent by rotary evaporation,

vi) re-dissolving the crude Δ^9 THC prepared in step v) in methanol, removing insoluble residue by filtration and removing solvent from the filtrate by rotary evaporation, and

vii) re-dissolving the crude Δ^9 THC prepared in step vi) in pentane, removing insoluble residue by filtration and removing solvent from the filtrate by rotary evaporation to give a semi-solid preparation of Δ^9 THC.

97. (New) A substantially pure preparation of Δ^9 tetrahydrocannabinol (Δ^9 THC) obtained by the method of claim 96, having a chromatographic purity of >99% by area normalisation of an HPLC profile.

98. (New) A method for producing Δ^9 tetrahydrocannabinol (Δ^9 THCV) crystals comprising:

i) obtaining an ethanolic solution of a botanical drug substance from cannabis plant material,

ii) passing the solution obtained in step i) through a column of activated charcoal, and collecting the eluate,

iii) remove solvent from the eluate by rotary evaporation to give a Δ^9 THCV enriched fraction,

iv) passing a solution of the resulting Δ^9 THCV enriched extract through a column packed with Sephadex LH20, eluting with 2:1 chloroform/dichloromethane,

v) collecting Δ^9 THCV rich fractions and removing solvent by rotary evaporation,

vi) re-dissolving the crude Δ^9 THCV prepared in step v) in methanol, removing insoluble residue by filtration and removing solvent from the filtrate by rotary evaporation, and

vii) re-dissolving the crude Δ^9 THC_V prepared in step vi) in pentane, removing insoluble residue by filtration and removing solvent from the filtrate by rotary evaporation to give said crystals of Δ^9 THC_V.

99. (New) A substantially pure preparation of Δ^9 tetrahydrocannabivarin (Δ^9 THC_V) obtained by the method of claim 98, having a chromatographic purity of greater than 95%, more preferably greater than 96%, more preferably greater than 97%, more preferably greater than 98%, and most preferably greater than 99% by area normalisation of an HPLC profile.

100. (New) A method for producing a highly enriched cannabigerol (CBG) extract or substantially pure CBG from cannabis plant material comprising:

- i) decarboxylating the cannabis plant material,
- ii) preparing an extract of the decarboxylated cannabis plant material with hexane,
- iii) filtering the resultant extract and removing solvent from the filtrate by rotary evaporation to form an extract enriched in CBG,
- iv) passing a solution of the resulting CBG enriched extract through a column packed with Sephadex-LH20™, eluting with 2:1 chloroform/dichloromethane,
- v) collecting CBG rich fractions eluted from the column and removing solvent by rotary evaporation,
- vi) re-dissolving the crude CBG obtained in step v) in methanol, removing insoluble residue by filtration and removing solvent from the filtrate by rotary evaporation, and
- vii) re-dissolving the product of step vi) in pentane, removing insoluble residue by filtration and removing solvent from the filtrate by rotary evaporation to produce a highly enriched CBG extract or substantially pure cannabigerol.

101. (New) A product enriched in cannabigerol (CBG) obtained by the method of claim 100, having a chromatographic purity of greater than 90%, preferably greater than 92% by area normalisation of an HPLC profile.

102. (New) A method of producing a highly enriched cannabichromene (CBC) extract from cannabis plant material comprising:

- i) decarboxylating the cannabis plant material,
- ii) preparing an extract of the decarboxylated cannabis plant material with hexane,

iii) filtering the resultant extract and removing solvent from the filtrate by rotary evaporation to form an extract enriched in CBC,

iv) passing a solution of the resulting CBC enriched extract through a column packed with Sephadex-LH20™, eluting with 2:1 chloroform/dichloromethane,

v) collecting CBC rich fractions eluted from the column and removing solvent by rotary evaporation,

vi) re-dissolving the crude CBC obtained in step v) in methanol, removing insoluble residue by filtration and removing solvent from the filtrate by rotary evaporation, and

vii) re-dissolving the product of step vi) in pentane, removing insoluble residue by filtration and removing solvent from the filtrate by rotary evaporation to produce a highly enriched CBC extract.

103. (New) A product enriched in cannabichromene (CBC) obtained by the method of claim 102, having a chromatographic purity of greater than 80%, more preferably greater than 85% by area normalisation of an HPLC profile.